

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C. 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 06 September 2000 (06.09.00)	
International application No. PCT/GB00/00226	Applicant's or agent's file reference N75751B GCW
International filing date (day/month/year) 26 January 2000 (26.01.00)	Priority date (day/month/year) 26 January 1999 (26.01.99)
Applicant VALLANCE, Patrick, John, Thompson et al	

1. The designated Office is hereby notified of its election made:

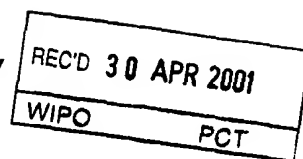
☒ in the demand filed with the International Preliminary Examining Authority on:14 August 2000 (14.08.00)☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Juan Cruz Telephone No.: (41-22) 338.83.38
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# PATENT COOPERATION TREATY

## PCT



### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference N.75751B GCW	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/00226	International filing date (day/month/year) 26/01/2000	Priority date (day/month/year) 26/01/1999
International Patent Classification (IPC) or national classification and IPC C12N9/78		
Applicant UNIVERSITY COLLEGE LONDON et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  14/08/2000	Date of completion of this report  26.04.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Bilang, J  Telephone No. +49 89 2399 8707



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00226

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-41 as originally filed

**Claims, No.:**

1-45 as originally filed

**Drawings, sheets:**

1/6-6/6 as originally filed

**Sequence listing part of the description, pages:**

1-14, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB00/00226

- ☐ the description,      pages:
- ☐ the claims,      Nos.:
- ☐ the drawings,      sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:  
**see separate sheet**

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 16-20, 22-26, 29, 31, 34-45 (completely), 1-12, 14, 15, 21, 27, 28, 30, 32, 33 (partially).

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
  - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
  - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
  - ☒ no international search report has been established for the said claims Nos. 16-20, 22-26, 29, 31, 34-45 (completely), 1-12, 14, 15, 21, 27, 28, 30, 32, 33 (partially).
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the standard.
  - ☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB00/00226

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**citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	3,4,11,12,14,15,21,30,32,33
	No: Claims	1,2,5-10,27,28
Inventive step (IS)	Yes: Claims	
	No: Claims	1-12,14,15,21,27,28,30,32,33
Industrial applicability (IA)	Yes: Claims	1-12,14,15,21,27,28,30,32,33
	No: Claims	

**2. Citations and explanations  
see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB00/00226

**Additional remarks Item I**

The priority appears to be validly claimed.

**Additional remarks Item III**

An objection under Article 3(4) PCT had been raised by the international Search Authority. This Authority agrees with the objection put forward by the ISA. The applicants did not pay any further search fees, and consequently the International Search Report had been issued for the invention first mentioned in the claims.

The international preliminary examination is limited to the claims for which a search report has been established (**Rule 66 (e) PCT**) i.e. for claims 1-12, 14, 15, 21, 27, 28, 30, 32, and 33 (all partially).

**Additional remarks Item V**

1. The present application discloses polypeptides having methylarginase activity (DDAH) and the polynucleotides encoding these polypeptides.

2. The following documents were taken into consideration:

D1: KIMOTO M. ET AL.: 'Purification, cDNA cloning and expression of human NG,NG-dimethylarginine dimethylaminohydrolase' EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 258, no. 2, December 1998, pages 863-868

D2: KIMOTO M. ET AL.: 'Detection of NG,NG-dimethylarginine dimethylaminohydrolase in human tissues using a monoclonal antibody' JOURNAL OF BIOCHEMISTRY, vol. 117, no. 2, February 1995, pages 237- 238

D3: LEIPER J.M. ET AL.: 'Identification of two human dimethylarginine dimethylaminohydrolases with distinct distribution and homology with microbial arginine deiminases' BIOCHEMICAL JOURNAL, vol. 343, October 1999, pages 209-214

3. In view of the disclosures of D1 and D2, the IPEA considers that the subject-matter of claims 1, 2, 5-10, 27 and 28 has been anticipated by the prior art and

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB00/00226

therefore contravene **Article 33(2)(3) PCT**.

- 3.1 D1 discloses the cDNA and amino acid sequence of a human dimethylaminohydrolase. The nucleotide sequence disclosed is 99,5% identical to the coding sequence of SEQ ID NO: 1; the proteins have 99,3% sequence identity. It can be understood from D3 (cited as technical evidence only) that D1 indeed discloses DDAH (p. 212, right col., 3rd line from bottom). The subject-matter of claims 1, 2, 5-9 thus is not novel over D1 (**Article 33(2) PCT**).
- 3.2 D1 furthermore discloses that antibodies raised against the rat enzyme cross reacted with the human enzyme (p. 865, left col. 2nd paragraph). D1 thus also anticipates the subject-matter of claim 10.  
The same objection could be based on D2.
4. The subject-matter of claims 1-12, 14, 15, 21, 27, 28, 30, 32, and 33, insofar as novel, is not based on an inventive activity in the sense of **Article 33(3) PCT**.

Based on the teachings of D1 it does not require any inventive skills to isolate allelic variants of the enzyme disclosed in D1. Moreover, once a cDNA is known, it does not require inventive skill to generate transgenic non-human animals, e.g. knock-out mice. The use of a known enzyme in methods for identifying modulators for that enzyme is also considered to belong to normal laboratory practise. Furthermore, the link between DDAH and diseases was also known (e.g. D1, p. 863, right col.). The use of the nucleic acid encoding DDAH or the DDAH itself in medicine therefore also appears to be obvious.

5. Claims 30 and 33 concern methods for the treatment of the human or animal body. For the assessment of said claims on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. In accordance with **Rul 67.1 (iv) PCT**, no opinion will therefore be given on the industrial applicability of said claims 30 and 33.
6. Note has been taken of the applicant's letter dated 17.04.2001. It should be noted, however, that this International Preliminary Examination Report is limited to the

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB00/00226

subject-matter for which an International Search Report has been established, i.e. human DDAH1. It is thus not an issue for the present Report whether it was known that more than one gene exists in humans and whether bacterial homologs were known.

**Additional remarks Item VIII**

1. Claim 4 covers a polynucleotide which comprises at least a fragment of the coding sequence of SEQ ID NO: 1. One nucleotide is considered to be a fragment of a given sequence. Claim 4 thus covers any polynucleotide.  
The reference to "fragments" is unclear even if fragments of some nucleotides are considered. It is not clear whether such fragments are novel and what their technical effects are.
2. Claim 5 embraces polypeptides which have methylarginase activity and which comprise a sequence substantially homologous to at least a fragment of SEQ ID NO: 2.  
The term "substantially homologous" is open to interpretation and thus not suitable to define the subject-matter for which protection is sought. It is not clear whether 50% or 75% or 95% "homology" would be considered to be "substantial".